

### REMARKS

The sequence listing is amended to correct SEQ ID NO:1. Support for the amendment can be found in the original specification at page 9, line 3. This part of the specification is also amended to read as original filed, and not as amended in the paper filed Oct. 22, 2001.

The Applicants cancel claims 16, and 29-43 without prejudice to subsequent prosecution. The Applicants have amended claims 19 and 20. Claim 19 is limited to a milk composition that comprises a Derp5 allergen. Claim 44 is new and, like claim 20, is a method of decreasing the production of IgE in a subject. Accordingly, the method of claim 44 is within the elected restriction group. Support for claim 45 can be found, e.g., at the paragraph beginning at page 10, line 15.

#### Rejections for Lack of Enablement

The Examiner rejected claims 16, 19-20, and 29-43 for lack of enablement. Applicants respectfully disagree and reserve the right to argue this rejection in subsequent prosecution. However, to expedite prosecution, the Applicants have amended claims 19 and 20 to recite a Derp5 allergen that comprises SEQ ID NO:1. The Examiner has found that methods of "oral feeding of a milk composition comprising a *Dermatophagoides pteronyssinus* allergen wherein said allergen is Der p5 of SEQ ID NO:3" are enabled. Paragraph 8, page 3, of the Action Dated March 24, 2003. The Applicants infer that the Examiner was referring to SEQ ID NO:1, which is the sequence listing for Der p5. See page 9 of the specification. Accordingly, at least claims 19 and 20 as presently amended are fully enabled. The Applicants respectfully request that the Examiner withdraw the rejection for lack of enablement as moot.

#### Rejections for Lack of Written Description

The Examiner rejected claims 16, 19-20, and 29-43 for lack of written description. Applicants again respectfully disagree and reserve the right to argue this rejection in subsequent prosecution. As presently amended, claims 19 and 20 recite a Derp5 allergen that comprises

SEQ ID NO:1. Accordingly, the Applicants respectfully request that the Examiner withdraw the rejection for lack of written description as moot.

#### 102(b) Rejection of Claim 20

Claim 20 has been amended. The cited references do not teach or suggest at least one of the limitations of claim 20 as presently amended.

#### Obviousness Rejections

The Examiner has rejected claim 19 and 20 as obvious in view of two combinations of references, both of which include Sato and Lin. As noted by the Examiner, Lin teaches the amino acid sequence of a Der p5 allergen. Sato describes administering an extract of dust mite, to variable effect.

A prima facie case of obviousness requires that the prior art references when combined teach or suggest all the claim limitations. MPEP 2143. However, the Examiner has not cited any reference which demonstrates that a Der p5 protein when transgenically produced in a mammary gland is in a form suitable for inducing allergenic tolerance when administered orally.

For example, Sato does not mention how the extract of dust mite was prepared or in what form the proteins in the extract are present (e.g., whether they present as hydrolyzed peptides and so forth). For example, the extract may not contain a substantial amount of Der p5 in a form that resembles the transgenically produced protein as required by claim 20 as presently amended. Likewise, since the extract is a complex mixture, Sato does not attribute the variable effects of orally administering the extract to Der p5.

Lin does not remedy the deficiencies of Sato. Lin teaches that Der p5 is a mite allergen, but does not teach that oral administration of a milk that includes Der p5 when transgenically produced in a mammary gland is in a form suitable for inducing immunological tolerance when administered orally.

U.S. 5,951,984 describes providing an antigen-containing preparation and contemplates that milk proteins and protein extracts of "host dust" as components of an antigen-containing

preparation. However, the '984 patent also does not demonstrate that a protein (nor a Der p5 protein, in particular) when transgenically produced in a mammary gland is in a form suitable for inducing immunological tolerance when administered orally.

U.S. 5,814,345 describes a milk that includes immune suppressive factor. The '345 patent discusses how an allergen can be administered to a milk-producing animal as protein. See, e.g., column 6, line 45. For example, the allergen is administered intramuscularly. See column 10, line 51. The milk-producing animal then apparently processes allergen administered to the animal into "a form which is secreted in the milk of the animal." See, e.g., column 6, lines 37-40. This allergen is in a "derivatized, processed form." See, e.g., column 5, line 44. Since the allergen is administered to the mammal as a protein rather than using a transgene that directs expression to the mammary gland, the '345 patent does not teach whether a protein (nor a Der p5 protein, in particular) transgenically produced in the mammary gland of a mammal would be in a suitable form for inducing immunological tolerance.

Wall describes the ability of transgenic animals to produce milk with foreign proteins. However, Wall does not teach whether a protein (nor a Der p5 protein, in particular) transgenically produced in the mammary gland of a mammal would be in a suitable form for inducing immunological tolerance.

Because no reference teaches that a protein transgenically produced in the mammary gland of a mammal would be in a suitable form for inducing immunological tolerance, the combination of references provided by the Examiner do not establish a prima facie case of obviousness. Moreover, none of the references provide any expectation for success that a milk composition containing an allergen transgenically produced in a mammary gland would be effective for inducing immunological tolerance.

The Applicants respectfully submit that the claims are in condition for allowance, which action is requested.

Applicant : Ching-Hsiang Hsu et al.

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Enclosed is a \$465 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: \_\_\_\_\_

9-29-03

Y. Rocky Tsao  
Y. Rocky Tsao  
Reg. No. 34,053

Fish & Richardson P.C.  
225 Franklin Street  
Boston, MA 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

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